AMENDMENTS TO THE CLAIMS

Pursuant to 37 C.F.R. 1.121 the following is a complete listing of the claims of the present application, depicting amendments; it replaces all previous versions.

Listing of the claims:

1.-45. (Canceled)

46. (Previously presented) A method of inhibiting Flt4 receptor tyrosine kinase (Flt4) function in a mammalian organism with a neoplastic disease, comprising administering to said mammalian organism a composition,

wherein said neoplastic disease is a breast carcinoma characterized by expression of Flt4 in vascular endothelial cells,

wherein said composition comprises an inhibitor of the binding of an Flt4 ligand protein to Flt4 expressed in blood vascular endothelial cells of said organism, wherein the inhibitor comprises a bispecific antibody, or fragment thereof, wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen, selected from the group consisting of PAL-E, VEGFR-1, and VEGFR-2,

wherein the composition is administered to the organism in an amount effective to inhibit Flt4 function in the organism.

47. (Canceled)

48. (Previously presented) A method according to claim 46 wherein said inhibitor further comprises an anti-neoplastic agent conjugated to said bispecific antibody or fragment thereof.

49-61. (Canceled)

62. (Previously presented) A method of treating a mammal having breast cancer characterized by blood vessel endothelial cells that express Flt4 tyrosine kinase (Flt4), comprising administering to said mammal a composition, said composition comprising an

inhibitor of binding between Flt4 ligand protein and Flt4 expressed in cells of said mammal, thereby inhibiting Flt4 function, where the inhibition of Flt4 function treats breast cancer,

wherein the inhibitor comprises a bispecific antibody, or fragment thereof, wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen.

63. (Previously presented) A method according to claim 62 wherein said mammal is human.

64. (Previously presented) A method according to claim 62 comprising a screening step preceding the administering step, wherein the screening step comprises screening a human to identify breast cancer characterized by blood vessel endothelial cells expressing Flt4; and

wherein the administering step comprises administering the composition to a human identified by the screening step as having breast cancer characterized by blood vessel endothelial cells expressing Flt4.

65-66. (Canceled)

67. (Previously presented) A method for treating a neoplastic disorder in a human subject, comprising:

(a) screening a human subject to identify a neoplastic disorder characterized by blood vessel endothelial cells expressing Flt4 receptor tyrosine kinase (Flt4); and

(b) administering a composition to a human subject identified according to (a) as having a neoplastic disorder characterized by blood vessel endothelial cells expressing Flt4, to inhibit Flt4 mediated proliferation of said Flt4-expressing cells, where inhibition of said proliferation treats the neoplastic disorder,

wherein the composition comprises a means for inhibiting Flt4 function in mixture with a pharmaceutically acceptable diluent, adjuvant, or carrier, wherein the means for inhibiting comprises a member selected from the group consisting of:

(i) an anti-Flt4 antibody or a polypeptide comprising an antigen binding fragment of said anti-Flt4 antibody;

(ii) an anti-VEGF-C antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-C antibody;

(iii) an anti-VEGF-D antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-D antibody;

(iv) a soluble polypeptide comprising a fragment of Flt4, wherein the polypeptide and the fragment are capable of binding to human VEGF-C (SEQ ID NO: 21); and

(v) a polypeptide comprising an Flt4 binding fragment of human prepro-VEGF-C (SEQ ID NO: 21) or human prepro-VEGF-D (SEQ ID NO: 22) conjugated to an antineoplastic agent.

68. (Previously presented) A method for treating a neoplastic disorder in a human subject, comprising:

(a) screening a human subject to identify a neoplastic disorder characterized by blood vessel endothelial cells expressing Flt4 receptor tyrosine kinase (Flt4); and

(b) administering a composition to a human subject identified according to (a) as having a neoplastic disorder characterized by blood vessel endothelial cells expressing Flt4, to inhibit Flt4 mediated proliferation of said Flt4-expressing cells, where inhibition of said proliferation treats the neoplastic disorder,

wherein the composition comprises a means for inhibiting Flt4 function in mixture with a pharmaceutically acceptable diluent, adjuvant, or carrier, wherein the means for inhibiting comprises a bispecific antibody, or fragment thereof, wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen.

69. (Previously presented) A method according to claim 68 wherein said blood vascular endothelial marker antigen is selected from the group consisting of PAL-E, VEGFR-1, and VEGFR-2.

70. (Previously presented) A method according to claim 68 wherein the means for inhibiting further comprises an anti-neoplastic agent conjugated to said bispecific antibody or fragment thereof.

71. (Canceled)

72. (Previously presented) A method of inhibiting proliferation of blood vessel endothelial cells in a mammalian organism having a disease characterized by expression of Flt4 tyrosine kinase (Flt4) in blood vessel endothelial cells, comprising administering to said mammalian organism a composition, said composition comprising an inhibitor of the binding of an Flt4 ligand protein to Flt4 expressed in blood vessel endothelial cells of said organism, thereby inhibiting Flt4-mediated proliferation of the blood vessel endothelial cells,

wherein the inhibitor comprises a bispecific antibody, or fragment thereof, wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen.

73. (Previously presented) A method of inhibiting proliferation of endothelial cells in a human organism having a disease characterized by expression of Flt4 tyrosine kinase (Flt4) in endothelial cells, comprising administering to said human organism a composition, said composition comprising an inhibitor of the binding of an Flt4 ligand protein to Flt4 expressed in endothelial cells of said organism, thereby inhibiting Flt4-mediated proliferation of the cells, wherein the inhibitor comprises a bispecific antibody, or fragment thereof, wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen.

74. (Previously presented) A method according to claim 72 or 73, wherein said blood vascular endothelial marker antigen is selected from the group consisting of PAL-E, VEGFR-1, and VEGFR-2.

75. (Previously presented) A method according to claim 72 or 73, wherein said inhibitor further comprises an anti-neoplastic agent conjugated to said bispecific antibody or fragment thereof.

76. (Canceled)

77. (Previously presented) A method of inhibiting proliferation of blood vessel endothelial cells in a mammalian organism having a breast carcinoma characterized by expression of Flt4 tyrosine kinase (Flt4) in blood vessel endothelial cells, comprising administering to said mammalian organism a composition, said composition comprising an inhibitor of the binding of an Flt4 ligand protein to Flt4 expressed in blood vessel endothelial cells of said organism, thereby inhibiting Flt4-mediated proliferation of the blood vessel endothelial cells,

wherein the inhibitor comprises a bispecific antibody, or fragment thereof, wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen.

78. (Previously presented) A method of inhibiting proliferation of endothelial cells in a human organism having a breast carcinoma characterized by expression of Flt4 tyrosine kinase (Flt4) in vascular endothelial cells, comprising administering to said human organism a composition, said composition comprising an inhibitor of the binding of an Flt4 ligand protein to Flt4 expressed in endothelial cells of said organism, thereby inhibiting Flt4-mediated proliferation of the cells, wherein the inhibitor comprises a bispecific antibody, or fragment thereof, wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen.

79. (Previously presented) A method according to claim 78 wherein said blood vascular endothelial marker antigen is selected from the group consisting of PAL-E, VEGFR-1, and VEGFR-2.

80. (Previously presented) A method according to claim 78 wherein said inhibitor further comprises an anti-neoplastic agent conjugated to said bispecific antibody or fragment thereof.

81. (Previously presented) A method of inhibiting genesis of blood vessels in a mammalian organism having a disease characterized by expression of Flt4 tyrosine kinase (Flt4) in blood vessels, comprising administering to said mammalian organism a composition, said composition comprising an inhibitor of the binding of an Flt4 ligand protein to Flt4 expressed in cells of said organism, in an amount effective to inhibit Flt4-mediated proliferation of said blood vessels in the organism, wherein said inhibitor comprises a member selected from the group consisting of:

(a) an anti-Flt4 antibody or a polypeptide comprising an antigen binding fragment of said anti-Flt4 antibody;

(b) an anti-VEGF-C antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-C antibody;

(c) an anti-VEGF-D antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-D antibody;

(d) a soluble polypeptide comprising a fragment of Flt4, wherein the polypeptide and the fragment are capable of binding to human VEGF-C (SEQ ID NO: 21); and

(e) a polypeptide comprising an Flt4 binding fragment of human prepro-VEGF-C (SEQ ID NO: 21) or human prepro-VEGF-D (SEQ ID NO: 22) conjugated to an antineoplastic agent.

82. (Previously presented) A method of inhibiting genesis of blood vessels in a mammalian organism having a disease characterized by expression of Flt4 tyrosine kinase (Flt4) in blood vessels, comprising administering to said mammalian organism a composition, said composition comprising an inhibitor of the binding of an Flt4 ligand protein to Flt4 expressed in cells of said organism, in an amount effective to inhibit Flt4-mediated proliferation of said blood vessels in the organism,

wherein the inhibitor comprises a bispecific antibody, or fragment thereof, wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen.

83. (Previously presented) A method according to claim 81 or 82 wherein said organism is human.

84. (Previously presented) A method according to claim 83, wherein the human has a tumor characterized by blood vessels that express Flt4.

85. (Previously presented) A method of inhibiting the growth or the metastatic spread of a tumor in a mammalian organism, comprising administering to a mammalian organism a composition that comprises an inhibitor of the binding of an Flt4 ligand protein to Flt4 receptor tyrosine kinase (Flt4) expressed in cells of said organism, wherein the mammalian organism has a tumor characterized by blood and lymphatic vessels that express Flt4, and wherein the composition inhibits proliferation of the blood and lymphatic vessels, thereby inhibiting growth or metastatic spread of the tumor, wherein the inhibitor comprises a member selected from the group consisting of:

(a) an anti-Flt4 antibody or a polypeptide comprising an antigen binding fragment of said anti-Flt4 antibody;

(b) an anti-VEGF-C antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-C antibody;

(c) an anti-VEGF-D antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-D antibody;

(d) a soluble polypeptide comprising a fragment of Flt4, wherein the polypeptide and the fragment are capable of binding to human VEGF-C (SEQ ID NO: 21); and

(e) a polypeptide comprising an Flt4 binding fragment of human prepro-VEGF-C (SEQ ID NO: 21) or human prepro-VEGF-D (SEQ ID NO: 22) conjugated to an antineoplastic agent.

86. (Previously presented) A method of inhibiting the growth or the metastatic spread of a tumor in a mammalian organism, comprising administering to a mammalian organism a composition that comprises an inhibitor of the binding of an Flt4

ligand protein to Flt4 receptor tyrosine kinase (Flt4) expressed in cells of said organism, wherein the mammalian organism has a tumor characterized by blood and lymphatic vessels that express Flt4, and wherein the composition inhibits proliferation of the blood and lymphatic vessels, thereby inhibiting growth or metastatic spread of the tumor,

wherein the inhibitor comprises a bispecific antibody, or fragment thereof, wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen.

87. (Previously presented) A method according to claim 85 or 86, comprising a diagnosing step prior to the administering step, said diagnosing step comprising identifying a mammalian organism that is a human having a tumor characterized by blood vessels that express Flt4.

88. (Previously presented) A method according to claim 87, comprising a diagnosing step prior to the administering step, said diagnosing step comprising identifying a mammalian organism that is a human having lymph node metastasis of a tumor, wherein the lymph node comprises cells expressing Flt4.

89. (Previously presented) A method of inhibiting neoplastic cell growth in a human subject, comprising:

(a) screening a human subject to identify a neoplastic disorder characterized by blood vessels that comprise endothelial cells expressing Flt4 receptor tyrosine kinase (Flt4); and

(b) administering a composition to a human subject identified according to (a) as having a neoplastic disorder characterized by blood vessels that comprise endothelial cells expressing Flt4, said composition comprising an inhibitor of the binding of an Flt4 ligand protein to Flt4 expressed in cells of said subject, in an amount effective to inhibit Flt4-mediated proliferation of said Flt4-expressing cells and inhibit neoplastic cell growth in the subject, wherein the inhibitor comprises a member selected from the group consisting of:

(i) an anti-Flt4 antibody or a polypeptide comprising an antigen binding fragment of said anti-Flt4 antibody;

(ii) an anti-VEGF-C antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-C antibody;

(iii) an anti-VEGF-D antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-D antibody;

(iv) a soluble polypeptide comprising a fragment of Flt4, wherein the polypeptide and the fragment are capable of binding to human VEGF-C (SEQ ID NO: 21); and

(v) a polypeptide comprising an Flt4 binding fragment of human prepro-VEGF-C (SEQ ID NO: 21) or human prepro-VEGF-D (SEQ ID NO: 22) conjugated to an antineoplastic agent.

90. (Previously presented) A method of inhibiting neoplastic cell growth in a human subject, comprising:

(a) screening a human subject to identify a neoplastic disorder characterized by blood vessels that comprise endothelial cells expressing Flt4 receptor tyrosine kinase (Flt4); and

(b) administering a composition to a human subject identified according to (a) as having a neoplastic disorder characterized by blood vessels that comprise endothelial cells expressing Flt4, said composition comprising an inhibitor of the binding of an Flt4 ligand protein to Flt4 expressed in cells of said subject, in an amount effective to inhibit Flt4-mediated proliferation of said Flt4-expressing cells and inhibit neoplastic cell growth in the subject,

wherein the inhibitor comprises a bispecific antibody, or fragment thereof, wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen.

91. (Previously presented) A method of inhibiting neoplastic cell growth in a mammalian subject, comprising:

(a) screening a mammalian subject to identify a neoplastic disorder characterized by blood vessel endothelial cells expressing Flt4 receptor tyrosine kinase (Flt4), wherein the screening comprises

(i) contacting tissue from the mammalian subject with a composition comprising an antibody or antibody fragment that specifically binds Flt4;

(ii) detecting said antibody or antibody fragment bound to cells in said tissue; and

(iii) screening for a neoplastic disorder from the quantity or distribution of said antibody or antibody fragment bound to cells in said tissue, wherein the detection of said antibody or antibody fragment bound to blood vessel endothelial cells is correlated with the presence of a neoplastic disease; and

(b) administering a composition to a mammalian subject identified according to (a) as having a neoplastic disorder characterized by blood vessel endothelial cells expressing Flt4, said composition comprising an inhibitor of the binding of an Flt4 ligand protein to Flt4 expressed in cells of said subject, thereby inhibiting Flt4-mediated proliferation of said Flt4-expressing cells and inhibiting neoplastic cell growth in the subject, wherein the inhibitor comprises a member selected from the group consisting of:

(i) an anti-Flt4 antibody or a polypeptide comprising an antigen binding fragment of said anti-Flt4 antibody

(ii) an anti-VEGF-C antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-C antibody;

(iii) an anti-VEGF-D antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-D antibody;

(iv) a soluble polypeptide comprising a fragment of Flt4, wherein the polypeptide and the fragment are capable of binding to human VEGF-C (SEQ ID NO: 21); and

(v) a polypeptide comprising an Flt4 binding fragment of human prepro-VEGF-C (SEQ ID NO: 21) or human prepro-VEGF-D (SEQ ID NO: 22) conjugated to an antineoplastic agent.

92. (Previously presented) A method of inhibiting neoplastic cell growth in a mammalian subject, comprising:

(a) screening a mammalian subject to identify a neoplastic disorder characterized by blood vessel endothelial cells expressing Flt4 receptor tyrosine kinase (Flt4), wherein the screening comprises

(i) contacting tissue from the mammalian subject with a composition comprising an antibody or antibody fragment that specifically binds Flt4;

(ii) detecting said antibody or antibody fragment bound to cells in said tissue; and

(iii) screening for a neoplastic disorder from the quantity or distribution of said antibody or antibody fragment bound to cells in said tissue, wherein the detection of said antibody or antibody fragment bound to blood vessel endothelial cells is correlated with the presence of a neoplastic disease; and

(b) administering a composition to a mammalian subject identified according to (a) as having a neoplastic disorder characterized by blood vessel endothelial cells expressing Flt4, said composition comprising an inhibitor of the binding of an Flt4 ligand protein to Flt4 expressed in cells of said subject, thereby inhibiting Flt4-mediated proliferation of said Flt4-expressing cells and inhibiting neoplastic cell growth in the subject,

wherein the inhibitor comprises a bispecific antibody, or fragment thereof, wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen.

93. (Previously presented) A method according to claim 91 or 92, wherein said tissue comprises mammary tissue.

94. (Previously presented) A method of inhibiting genesis of blood vessels in a mammalian organism having a disease characterized by expression of Flt4 tyrosine kinase (Flt4) in blood vessels, comprising administering to said mammalian organism a composition, said composition comprising an inhibitor of the binding of an Flt4 ligand protein to Flt4 expressed in cells of said organism, thereby inhibiting Flt4-mediated proliferation of blood vessels in the organism that express Flt4, wherein said inhibitor comprises a soluble polypeptide comprising a fragment of Flt4, wherein the polypeptide and the fragment are capable of binding to human VEGF-C (SEQ ID NO: 21).

95. (Previously presented) A method according to claim 94 wherein said organism is human.

96. (Previously presented) A method according to claim 95, wherein the human has a tumor characterized by blood vessels that express Flt4.

97. (Previously presented) The method of any one of claims 67, 81, 85, 89 and 91, wherein the inhibitor is an anti-Flt4 antibody or a polypeptide comprising an antigen binding fragment of said anti-Flt4 antibody.

98. (Previously presented) The method of any one of claims 67, 81, 85, 89 and 91, wherein the inhibitor is a soluble polypeptide comprising a fragment of Flt4, wherein the polypeptide and the fragment are capable of binding to human VEGF-C (SEQ ID NO: 21).

99. (Previously presented) A method for antagonizing the function of Flt4 receptor tyrosine kinase (Flt4) in a mammalian organism, comprising administering to the organism a composition comprising a bispecific antibody, or fragment thereof, in an amount effective to antagonize the function of Flt4 in the mammal,

wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen; and

wherein said organism has a neoplastic disorder characterized by blood vessels comprising endothelial cells that express Flt4.

100. (Previously presented) The method according to claim 99, wherein the organism is human.

101. (Previously presented) The method according to claim 99, wherein said composition further comprises an anti-neoplastic agent conjugated to said antibody or antibody fragment.

102. (Currently amended) A method of inhibiting neoplastic cell growth in a mammalian subject, comprising:

(a) screening a mammalian subject to identify a neoplastic disorder characterized by blood vessels that comprise endothelial cells that express Flt4; and

(b) administering a composition to a mammalian subject identified according to (a) as having a neoplastic disorder characterized by blood cells expressing Flt4, said composition comprising an inhibitor of the binding of an Flt4 ligand protein to Flt4 expressed in cells of said subject, where the composition is administered in an amount effective to inhibit Flt4-mediated proliferation of said Flt4-expressing cells and inhibit neoplastic cell growth in the mammal, wherein said inhibitor comprises a polypeptide selected from the group consisting of:

(i) an anti-Flt4 antibody or a polypeptide comprising an antigen binding fragment of said anti-Flt4 antibody;

(ii) an anti-VEGF-C antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-C antibody;

(iii) an anti-VEGF-D antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-D antibody

(iv) a soluble polypeptide comprising a fragment of Flt4, wherein the polypeptide and the fragment are capable of binding to human VEGF-C (SEQ ID NO: 21); and

(v) a polypeptide comprising an Flt4 binding fragment of human prepro-VEGF-C (SEQ ID NO: 21) or human prepro-VEGF-D (SEQ ID NO: 22) conjugated to an antineoplastic agent.

103. (Previously presented) A method of treating a mammal having breast cancer characterized by blood vessel endothelial cells that express Flt4 tyrosine kinase (Flt4), comprising administering to said mammal a composition, said composition comprising an inhibitor of binding of an Flt4 ligand protein to Flt4 expressed in cells of said organism, thereby inhibiting Flt4 function and treating the mammal, wherein the inhibitor comprises a member selected from the group consisting of:

(a) an anti-Flt4 antibody or a polypeptide comprising an antigen binding fragment of said anti-Flt4 antibody;

(b) an anti-VEGF-C antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-C antibody;

(c) an anti-VEGF-D antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-D antibody;

(d) a soluble polypeptide comprising a fragment of Flt4, wherein the polypeptide and the fragment are capable of binding to human VEGF-C (SEQ ID NO: 21); and

(e) a polypeptide comprising an Flt4 binding fragment of human prepro-VEGF-C (SEQ ID NO: 21) or human prepro-VEGF-D (SEQ ID NO: 22) conjugated to an antineoplastic agent.

104. (Previously presented) A method of treating a mammal having breast cancer characterized by blood vessel endothelial cells that express Flt4 tyrosine kinase (Flt4), comprising administering to said mammal a composition, said composition comprising an inhibitor of binding between Flt4 ligand protein and Flt4 expressed in cells of said organism, thereby inhibiting Flt4 function and treating the mammal,

wherein the inhibitor comprises a bispecific antibody, or fragment thereof, wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen.

105. (Previously presented) The method according to claim 103 or 104, wherein said mammal is human.

106. (Previously presented) The method according to claim 105, comprising a screening step preceding the administering step, wherein the screening step comprises screening a human to identify breast cancer characterized by blood vessel endothelial cells expressing Flt4; and

wherein the administering step comprises administering the composition to a human identified by the screening step as having breast cancer characterized by blood vessel endothelial cells expressing Flt4.

107. (Currently amended) A method of inhibiting neoplastic cell growth in a mammalian subject, comprising:

(a) screening a mammalian subject to identify a neoplastic disorder characterized by blood vessels that comprise endothelial cells that express Flt4; and

(b) administering a composition to a mammalian subject identified according to (a) as having a neoplastic disorder characterized by blood cells expressing Flt4, said composition comprising an inhibitor of the binding of an Flt4 ligand protein to Flt4 expressed in cells of said subject, thereby inhibiting Flt4-mediated proliferation of said Flt4-expressing cells and inhibiting neoplastic cell growth,

wherein said inhibitor comprises a bispecific antibody, or fragment thereof, wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen selected from the group consisting of PAL-E, VEGFR-1 and VEGFR-2.

108. (Previously presented) The method according to claim 107, wherein the mammalian subject is human.

109. (Previously presented) The method according to claim 107, wherein said inhibitor further comprises an anti-neoplastic agent conjugated to said bispecific antibody.

110. (Previously presented) The method according to claim 107 wherein the screening comprises:

(a) contacting tissue from the mammalian subject with a composition comprising an antibody or antibody fragment that specifically binds Flt4;

(b) detecting said antibody or antibody fragment bound to cells in said tissue; and

(c) screening for a neoplastic disorder characterized by blood vessels that comprise endothelial cells that express Flt4 from the quantity or distribution of said antibody bound to cells in said tissue.

111. (Previously presented) The method according to claim 110, wherein in said screening, the detection of said antibody or antibody fragment bound to blood vessel endothelial cells is correlated with the presence of a neoplastic disease.

112. (Previously presented) The method according to claim 110 wherein said tissue comprises mammary tissue.

113. (Previously presented) A method of treating a human subject comprising:

(a) screening a human subject to identify tumor blood vasculature that expresses Flt4 tyrosine kinase (Flt4), and

(b) administering to a subject identified by such screening as having tumor blood vasculature that expresses Flt4 a composition that comprises an inhibitor of binding between an Flt4 ligand and Flt4, in an amount effective to inhibit Flt4-mediated proliferation of said blood vasculature in the subject,

wherein said inhibitor comprises a member selected from the group consisting of:

(i) an anti-Flt4 antibody or a polypeptide comprising an antigen binding fragment of said anti-Flt4 antibody;

(ii) an anti-VEGF-C antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-C antibody;

(iii) an anti-VEGF-D antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-D antibody;

(iv) a soluble polypeptide comprising a fragment of Flt4, wherein the polypeptide and the fragment are capable of binding to human VEGF-C (SEQ ID NO: 21); and

(v) a polypeptide comprising an Flt4 binding fragment of human prepro-VEGF-C (SEQ ID NO: 21) or human prepro-VEGF-D (SEQ ID NO: 22) conjugated to an antineoplastic agent.

114 - 115. (Canceled)

116. (Previously presented) The method of claim 67, wherein the screening of the human subject to identify a neoplastic disorder characterized by blood vessel endothelial cells expressing Flt4 receptor tyrosine kinase (Flt4) comprises contacting cells from the subject with a Flt4 antibody or a polypeptide comprising an antigen binding fragment of said anti-Flt4 antibody, and detecting blood vessel endothelial cells stained with said antibody or polypeptide.

117. (Canceled)

118. (Previously presented) The method of claim 87, wherein the identifying comprises contacting cells from a human with a Flt4 antibody or a polypeptide comprising an antigen binding fragment of said anti-Flt4 antibody, and detecting blood vessel endothelial cells stained with said antibody or polypeptide, thereby diagnosing the human as having a tumor characterized by blood vessels that express Flt4.

119. (Previously presented) The method of claim 91, wherein the mammalian subject is human.

120. (Previously presented) The method of claim 97, wherein the anti-Flt4 antibody is a human or humanized antibody.

121. (Previously presented) The method of claim 102, wherein the screening of the mammalian subject to identify a neoplastic disorder characterized by blood vessels that comprise endothelial cells that express Flt4 comprises contacting cells from the organism with an anti-Flt4 antibody or a polypeptide comprising an antigen binding fragment of said anti-Flt4 antibody, and detecting blood vessel endothelial cells stained with said antibody or polypeptide.

122. (Previously presented) The method of any one of claims 102, 103, 113, and 114, wherein the inhibitor is an anti-Flt4 antibody or a polypeptide comprising an antigen binding fragment of said anti-Flt4 antibody.

123. (Previously presented) The method of claim 122, wherein the anti-Flt4 antibody is a human or humanized antibody.

124. (Previously presented) The method of any one of claims 102, 103, 113, and 114, wherein the inhibitor is a soluble polypeptide comprising a fragment of Flt4, wherein the polypeptide and the fragment are capable of binding to human VEGF-C (SEQ ID NO: 21).

125. (Previously presented) The method of any one of claims 67, 81, 85, 86, 89, 91, 102, 103, 113, and 114, wherein the inhibitor further comprises an anti-neoplastic agent conjugated thereto.

126. (Previously presented) The method of any one of claims 67, 81, 85, 86, 91, 102, 103, 113, and 114, wherein the composition further comprises a pharmaceutically acceptable diluent, adjuvant, or carrier.